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10/586,337

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EXAMINER

KELLY, ROBERT M

ART UNIT

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/586,337	<b>Applicant(s)</b> NISHIYAMA ET AL.	
	<b>Examiner</b> ROBERT M. KELLY	<b>Art Unit</b> 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 25 April 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1 and 3-13 is/are pending in the application.
- 4a) Of the above claim(s) 4-6, 11 and 12 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 3, 7-10, 13 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>7/14/06</u>   | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

Applicant's response and amendment of 4/25/08 is entered.

Claims 1, 3, and 7 are amended.

Claims 2 are cancelled.

Claim 13 is newly presented.

Claims 1, 3-12, and 13 are presently pending.

### ***Election/Restrictions***

Applicant's election without traverse of Invention I, Claims 1-10, and the species of *Candida*, encompassed in Claims 1-3 and 7-10 in the reply filed on 11/16/07 is acknowledged.

Claims 4-6 and 11-12 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions and species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/16/07.

Claims 1-3, 7-10, and 13 are presently considered.

### ***Information Disclosure Statement***

It is noted that Whitney Article does appear to be present in full form at this point. The Examiner does not understand why the error was made, however, to remove the problem, the Whitney Article is now initialed in the IDS, and a new copy is supplied.

It is further noted that Applicant argues that the three US patents co-listed in the search report submitted are each concise statements of the relevance of the Japanese language

document, and hence, the Japanese WIPO document is signed off on this basis (i.e, the disclosures of the cited US documents).

However, the Letunova document remains non-considered for reasons of record.

***Response to Argument – Letunova Document***

Applicant's argument of 4/25/08 has been fully considered but is not found persuasive.

Applicant argues that the submitted International Search Report constitutes a concise statement of the relevance of the foreign language references, and as such, the Examiner should sign off on, *inter alia*, the Letunova language document (p. 7, last paragraph).

Such is not persuasive. 37 CFR 1.98(a)(3)(i) requires a concise explanation of the relevance, as it is presently understood by the individual designated in 1.56(c) most knowledgeable about the content of the information, of each patent, publication, or other information listed that is not in the English language. The individuals designated in 37 CFR 1.56(c) are inventors of the Application, the Attorneys or Agents associated, and anyone substantively involved in preparation or prosecution of the application who is associated with the inventor, the assignee, or anyone to whom there is obligation to assign the Application. The search report in itself contains no description of the relevance, but merely a statement of the claims to which that Examiner found that it might be applied. No mention is made of how Letunova is relevant, just that it is so-relevant, and no explanation of the subject matter within the documents. The title of Letunova is the whole description of the document, which states "Preparation of [gamma]-acetopropyl alcohol from [gamma]-butyrolacetone", yet the Examiner knows nothing from this about the relevance of the Article. Moreover, the Examiner in the international Application is not involved in any way with the present Application's prosecution.

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Simply put, if the Examiner were to sign off on this document, he would be doing so on the basis that these documents exist in the record, not that he understood anything at all about the document. It is simply not reasonable to sign off on these documents under such circumstances. Such is because the decision to do so would create a presumption of consideration by the Examiner in a court of law, and the consideration would not be in any way proper as there is no description of the relevance, and any description of relevance was made by someone outside of the requirements of 37 CFR 1.56(c). The citations of the CFR above are rules made to avoid such problems. (See MPEP 609.01, et seq.; MPEP 609.05(a), et seq.)

### ***Claim Objections***

In light of the Argument, the objections to Claims 1-3 and 7-10 for various informalities are withdrawn.

To wit, further consideration has caused the Examiner to determine that Applicant actually means to claim more than the Artisan would have understood the claim to encompass, due to the specific definition of "enzyme source" in the specification.

### ***Double Patenting***

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The

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filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Applicant is advised that should claim 10 be found allowable, claim 13 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim 13 is clearly the combination of the limitations of Claim 10 and Claim 1, and Claim 10 depends from Claim 1. Hence, despite a slight difference in wording, the claims are substantial duplicates.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

While the rejection of Claim 1 as rejected under 35 U.S.C. 102(b) as being anticipated by Whitney, et al. (1972) Advances in Chemistry, Vol. 130: 270-80, under the basis previously given,

Claim 1 is newly rejected under 35 U.S.C. 102(b) as being anticipated by Whitney, et al. (1972) Advances in Chemistry, Vol. 130: 270-80, for reasons necessitated by amendment.

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Whitney teaches the reduction of 5-hydroxy-2-pentanone by chelated lithium compounds, to yield optically active 1,4-pentanediol (e.g., p. 277). Moreover, the compounds exhibit stereoselective reduction, otherwise the resultant compound would not be optically active. Hence, the claim is anticipated.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1 and 10 remain rejected, and Claim 13 is newly rejected, under 35 U.S.C. 103(a) as being unpatentable over Whitney, et al. (1974) *Advances in Chemistry*, Vol. 130: 270-80 and the general knowledge in the art,

With regard to Claim 1, as shown above, Whitney teaches one from of enzymatic reduction of the compound. However, Whitney does not teach obtaining the compound for reduction from a method comprising acid hydrolysis of 2-hydroxy-gamma-butyrolactone.

On the other hand, it is well known that 2-hydroxy-gamma-butyrolactone has been available for years, and even Applicant's specification that the availability of such is superior to other sources, evidencing Applicant's acknowledgement of the Art. This is Official Notice.

Second, it is instantly recognizable to the Artisan, who is aware of organic chemistry, that an acid hydrolysis, followed by a reduction by  $\text{LiAlH}_4$  will yield the alcohol of formula 2.

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Hence, at the time of the invention, the claimed invention would have been obvious. The Artisan would be motivated to perform the acid hydrolysis to perform a reduction and thereby obtain the compound of interest. Moreover, the Artisan would have had a reasonable expectation of success, as the art of organic chemistry was already fleshed out for the methods involved in such syntheses.

***Response to Argument – 103 - Whitney and general knowledge***

Applicant's argument of 4/25/08 has been fully considered but is not found persuasive.

Applicant argues that the Examiner has not provided reasoning why the Artisan would be motivated to employ 5-acetyl-gamma-butyrolactone as the source (p. 11, paragraph 2).

Such is not persuasive. The Examiner has stated that the motivation is found, because the compound is readily available and would be instantly understood to be able to make the compound for reduction. This hinges on the findings of *KSR v. Teleflex* 82 USPQ.2d 1385 (U.S. 2007). The court in such finding stated that motivation does not to be specific, and a rigid TSM approach is therefore rejected. Hence, the mere motivation is found in the availability of such compounds to the Artisan, rather than a specific statement or implication by a citation in the Art that the compound could be utilized as a source.

Applicant argues they have provided the motivation of avoiding degradation when stored at high purity, and hence, their limitation is non-obvious over the Art (p. 11, paragraph 3).

Such is not persuasive. The Examiner has provided other reasoning already in the Art to employ the compound. The Examiner's reasoning need not be the same as Applicant's. Still further, in *KSR v. Teleflex*, it is clear that the chief concern of the court was the obstruction of what was already available to the Artisan, and such why the rigid TSM test was rejected. Here,



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if the Examiner were to remove the rejection, the Artisan would be precluded from practicing the already available knowledge in the Art. Hence, the rejection is maintained.

Applicant argues that Whitney does not disclose the asymmetric reduction of the compound, as now recited in the method, and hence, Claim 10 is patentable.

Such is not persuasive. Because Whitney demonstrates optically active, it demonstrates asymmetric reduction, such is the core of Whitney.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

In light of Applicant's argument with regard to reasonable predictability, the rejections of Claims 1-3, 7, and 8 under 35 U.S.C. 103(a) as being unpatentable over Whitney, et al. (1974) *Advances in Chemistry*, Vol. 130: 270-80; and Wada, et al. (1998) *Biosci. Biotechnol. Biochem.*, 62(2): 280-85, are withdrawn.

To wit, Applicant has demonstrated that these enzymes work to selectively produce enantiomers in a manner that the Artisan cannot predict (i) if any particular substrate will work for any particular enzyme and (ii) which enantiomer will be produced if it works, and (iii) even if any product will be produced. The Examiner accepts Applicant's arguments.

### **New Rejections**

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 7-10 and 13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the enzymes encoded in pNTS1G, pNTFPG, pNTDRG1, pNTRS, and pNTRGG1, to produce R, R, R, S, and S enantiomers, respectively, does not reasonably provide enablement for the breadth of products (e.g., enzyme sources, enzymes) and the breadth of organisms and the breadth of enantiomers for any particular source. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The encompass the production of optically active 1,4-pentanediol from 5-hydroxy-2-pentanone, by any enzyme source having the activity of stereoselectively reducing the pentanone. The enzyme source can be any cultured product of various microorganisms (Claim 3), indicating that the enzyme source may be derived of any organism in the broad claims. The enzyme source can be of any genus *Candida* or *Devosia*, *Candida malis*, or *Candida magnoliae*, or any enzyme obtained from these to obtain the R-isomer (Claims 7-8), indicating that the broad claims encompass the use of these same enzyme sources to produce the S isomer. FERM BP-8535, 7117, or 08458, or any enzyme obtained from such may be used to produce the R isomer (Claim 9), indicating that the broad claims go beyond these specific deposits, as well as include a broad

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range of enzymes. Claims 10 and 11 are limited to the use of a specific precursor to obtain the pentanone, however, are also subject to the breadth of enzymes and sources and isomers.

The nature of the invention is the selective reduction of 5-hydroxy-2-pentanone with any enzyme to produce optically active 1,4-pentane diol. The invention is generally enabled for the use of standard organic chemistry methods, e.g., Whitney, et al. (1974) *Advances in Chemistry*, Vol. 130: 270-80. The organic chemist is well aware of organic chemistry, and the methods to produce the product are generally within the grasp of the organic chemist without undue experimentation. However, the claims also, importantly, encompass the use of biochemical enzymes (i.e., protein enzymes) to produce the same. This is where the problems in the Art exist.

The closest Prior Art with regard to biochemical reductions are those of Wada, et al. (1999) *Journal of Bioscience and Bioengineering*, 87(2): 144-48 and Wada, et al. (1998) *Bioscience and Biotechnological Biochemistry*.

The Wada (1998) article teaches and reviews a general characterization of several enzymes from various organisms, which produce stereoselective reductions of a distinct molecule, which have stereoselectivity which is not commensurate with any specific enantiomer, such that, from this Article, the Artisan could not reasonably predict that any particular enantiomer would be made in any specific organism (DISCUSSION), other than that the specific enzyme will produce the product found.

The Wada (1999) article teaches several enzymes derived from a specific species of *Candida* which have distinct activities with regard to the reduction of specific chemicals (e.g., TABLE 2).

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However, commensurate with Applicant's argument of 4/25/08 (pp. 12-13), it is clear that Wada also notes that several substrates will not work with specific enzymes, and there is simply no way to reasonably predict which of the enzymes, or which other enzymes will produce the activity required of reducing the pentanones and with the stereoselectivity required, in any specific embodiment.

Applicant's specification Broadly teaches many sources of enzyme and broadly states that these enzymes may be used to obtain the various isomers with the various stereoselectivity.

Applicant's examples teach specific encoded deposits of enzymes pNTS1G, pNTFPG, pNTDRG1, pNTRS, and pNTRGG1, without reference to which enzyme is which, and from where it is obtained. Hence, the Examiner cannot determine more from this than that the specific enzymes will work.

Still further, it is clear from the specification, that the enzyme source is self-determining (e.g., definition of Enzyme Source, p. 14), without any more elaboration as to which enzyme sources actually have the activity.

Therefore, the Artisan would have to experiment to find those sources that would produce the required reduction, and determine which isomer would be produced (i.e., S or R), as well as determine those enzymes encompassed which produce the particular activity.

Such experimentation is considered undue as it is required to reasonably predict the breadth of Applicant's claimed invention for Applicant.

### ***Conclusion***

No Claim is allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT M. KELLY whose telephone number is (571)272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert M Kelly/  
Examiner of Art Unit 1633